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Composite pH Predicts Esomeprazole Response in Laryngopharyngeal Reflux Without Typical Reflux Syndrome

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Objectives/Hypothesis: Factors predicting the efficacy of proton pump inhibitors (PPIs) in patients with suspected laryngopharyngeal reflux (LPR) are unclear. PPI treatment in patients without concomitant esophageal syndrome remains controversial. We investigated whether composite pH can predict PPI treatment response for LPR with or without concomitant typical reflux syndrome (CTRS).

Study Design: Prospective, open-label therapeutic cohort study.

Methods: Patients with LPR in a tertiary center divided by presence (n = 65) and absence (n = 42) of CTRS underwent 24-hour esophagopharyngeal pH test and took esomeprazole (40 mg, twice daily) for 12 weeks. Positive composite pH was defined as the presence of 1) excessive pharyngeal acid reflux, and/or 2) excessive distal esophageal acid reflux. A responder was defined as a patient with ≥50% reduction in primary laryngeal symptoms. The change in reflux symptoms was determined using the reflux symptom index (RSI) questionnaire. Logistic regression and mixed model were used to evaluate the predictability of the composite pH parameter.

Results: After 8 and 12 weeks of treatment, participants with positive composite pH were 10.3-fold (95% confidence interval [CI], 1.7–61.5; $P = .01$) and 7.9-fold (95% CI, 1.4–44.8; $P = .02$) more likely to respond, respectively, than participants with negative composite pH among patients without CTRS. However, no difference was found in those with CTRS. Weekly repeated measures of RSI yielded similar findings.

Conclusions: In patients with suspected LPR without CTRS, a composite pH parameter, which incorporates pharyngeal and distal esophageal acid reflux, may predict response to esomeprazole therapy.

Key Words: Laryngopharyngeal reflux, pH parameter, proton pump inhibitors, treatment effectiveness.

Level of Evidence: 2b

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INTRODUCTION

The prevalence of laryngopharyngeal reflux (LPR) is estimated to be 4% to 10% among patients who consult otolaryngologists for reflux-related complaints.[1] Proton pump inhibitors (PPIs) have been recommended for the treatment of LPR.[2] However, their efficacy for relieving laryngeal symptoms remains unproven.[3] Overdiagnosis may account for the controversy, because neither symptoms nor signs of larynx are specific for the diagnosis.[4] The uncertainty of diagnosis and treatment efficacy has resulted in high costs, low patient satisfaction, and frustrated physicians. Therefore, it is crucial to identify potential predictors of treatment response to PPIs.

The American Gastroenterological Association guidelines recommend that empirical treatment with PPIs for LPR should be based on the presence of concomitant esophageal reflux syndrome.[2] However, the American Academy of Otolaryngology has stated that most patients do not have heartburn or reflux esophagitis.[5] The discrepancy raises the possibility of different patient populations being seen by physicians specializing in different fields; for example, concomitant typical reflux syndrome (CTRS) may be more frequently seen in gastroenterology clinics, whereas chronic laryngitis patients without CTRS may be more likely to visit an otolaryngologist. Given that patients without CTRS are less likely to have background reflux, the 24-hour pH test may be

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useful for predicting the treatment response in patients who are not indicated for antisecretory agents according to the current gastroenterology guidelines.[2]

Despite being able to differentiate LPR patients from normal controls,[6] the pH test does not predict the treatment response to PPIs in most placebo-controlled trials.[3] Most of these trials suffered from small sample size, and included both patients with and patients without CTRS. The largest controlled trial (146 subjects), conducted by Vaezi et al., is the only study to have recruited subjects without CTRS.[7] There was no evidence supporting the ability of the pH test to predict esomeprazole treatment response. However, pH data were only available for less than half of the participants (65 for distal esophagus and 62 for pharynx), and a composite pH (cpH) parameter, incorporating esophagus and pharynx acid reflux, was not used for the prediction of treatment response in their study. The aforementioned methodological concern raises doubts about the diagnostic role of the pH test.

Because the mechanisms of LPR involve both the microaspiration of refluxate to the airway and a vagal-mediated esophagobronchial reflex,[8] we postulated that a composite pH parameter incorporating both pharyngeal and esophageal acid refluxes may predict the response to therapy with PPIs in patients without CTRS.

MATERIALS AND METHODS

This was a prospective, open-label therapeutic trial, conducted in accordance with good clinical practice and the Declaration of Helsinki. The protocol was approved by Taichung Veterans General Hospital's Institutional Review Board (#C06254) on January 29, 2007. All participants signed an informed consent form prior to the study.

Patient Selection

Patients (aged >18 years) consulting otolaryngologists at the Department of Otolaryngology clinic of Taichung Veterans General Hospital between January 2007 and December 2011 with suspected LPR were considered for study enrollment, including: throat clearing, cough, globus, sore throat, or hoarseness for at least 3 consecutive months before screening. To be eligible for inclusion in this study, patients were required to have: 1) the primary laryngeal symptoms rating no less than 2 points on a 0 to 3 Likert severity scale in two assessments performed 7 to 14 days apart at baseline; and 2) the laryngoscopic signs suspected of reflux such as posterior laryngitis, interarytenoid bar, granuloma, and erythema or edema of the larynx.

Patients were excluded for any of the following conditions: respiratory or gastrointestinal malignancy; radiation therapy or surgery of the head, neck, lung, or gastrointestinal tract; trauma or surgery near the larynx; current or history of heavy smoking; substance or alcohol abuse history; infectious laryngitis in the previous 3 months; exposure to environmental irritants in the past 3 months; vocal cord papilloma; enlarged lingual or palatine tonsils, or goiters; excessive voice use; bronchial asthma; chronic cough attributable to angiotensin-converting enzyme inhibitor; known chronic pulmonary or tracheobronchial etiologies, such as eosinophilic bronchitis, bronchiectasis, positive methacholine provocation test, or response to inhaled or systemic steroid; pharyngeal (Zenker) diverticulum or esophageal stasis syndrome, such as achalasia; anxiety or depression with response to at least 1 month of an anxiolytic or an antidepressant[9]; chronic or allergic rhinosinusitis, nasal polyposis, or postnasal drip with response to at least 1 month of medical therapy with antihistamine or topical steroid spray, or defined by nasal endoscopy or computed tomography scan; participation in another investigational drug study in the previous month; acid-suppressive therapy within 4 weeks prior to recruitment; and need for continuous therapy with theophylline, iron supplements, warfarin, antifungal drugs, or digitalis. The participants were also excluded if they could not tolerate PPIs or an ambulatory pH test, had a serious illness that would interfere with study participation, or refused to participate. Women were required to be nonpregnant and nonlactating and to maintain effective contraception if of child-bearing potential.

Screening Period

Participants who met the eligibility criteria were enrolled in a 2- to 4-week run-in period to ensure compliance. Among the five laryngeal symptoms (hoarseness, throat clearing, sore throat, globus, and cough), the participants were asked to identify the single most bothersome symptom as the primary laryngeal symptom. The presence or absence of CTRS was evaluated based on the definition of mild symptoms of heartburn and/or regurgitation occurring at least twice a week, or moderate/severe symptoms that occurred at least once a week,[10] using the Taiwan version of a simplified gastroesophageal reflux disease questionnaire.[11] This questionnaire was the modified version of a previously published internationally validated questionnaire.[12]

Study Design

Both participants and investigators were blind to the results of upper gastrointestinal endoscopy and 24-hour pH monitoring. After the completion of all examinations, the participants were diagnosed with chronic laryngitis probably due to reflux, which requires 12 weeks of twice daily PPI therapy. The participants were instructed to take an oral esomeprazole tablet (40 mg; Nexium; AstraZeneca Pharmaceuticals, Södertälje, Sweden) 30 minutes before breakfast and 30 minutes before dinner. During the treatment period, patients' adherence to treatment, adverse events, and concomitant medication were evaluated and documented at 4-, 8-, and 12-week follow-up visits.

Laryngoscopy

Laryngoscopy was performed using a flexible nasolaryngoscope (VNL-1171K; Pentax, Tokyo, Japan) at enrollment by the same laryngologist (C.-C.W.). The laryngeal signs were documented at baseline and after 12 weeks of treatment based on the reflux finding score.[13]

Upper Gastrointestinal Endoscopy

All participants underwent diagnostic upper gastrointestinal endoscopy to evaluate the presence of reflux esophagitis and other mucosal lesions. Reflux esophagitis was defined according to the Los Angeles classification.

Twenty-Four–Hour Ambulatory Esophagopharyngeal pH Monitoring

An ambulatory 24-hour pH catheter incorporating three antimony sensors into a bifurcated probe with a single connector was used (Sandhill Scientific, Highlands Ranch, CO). A detailed description of the technique has been described previously.[14] Briefly, manometry was used to position the proximal sensor 1 cm above the upper esophageal sphincter, the middle sensor at 10 cm distal to the proximal one, and the distal sensor

at 5 cm above the lower esophageal sphincter. The participants consumed their usual diet but excluded citrus fruit, acidic beverages, carbonated beverages, caffeinated beverages, and any antireflux medications including PPIs.

Interpretation of pH Parameters

An abnormal cpH criterion was defined as the presence of 1) ≥2 episodes of pharyngeal acid reflux and/or 2) excessive distal esophageal acid reflux, that is, ≥4.6% of total acid exposure time with pH <4 at 5 cm above the upper margin of the lower esophageal sphincter.[15] The percentage of total time with pH <4 has been proved as a single reliable and accurate parameter in the diagnosis of gastroesophageal reflux disease.[16] We adopted a strict criterion, developed by Williams et al.,[17] with slight modification to define an event of pharyngeal acid reflux. The details have been described elsewhere.[14] Because one episode of pharyngeal acid reflux may be present in 10% to 20% of normal volunteers using the same pH catheter technique, we define excessive pharyngeal acid reflux as ≥2 reflux episodes within 24 hours after excluding artifacts.[18]

Outcome Measures

Two outcome measures were used to evaluate the PPI treatment response. The primary outcome was the response to PPIs, defined as a ≥50% reduction in primary laryngeal symptoms, which differentiated responders from nonresponders and was measured using a 10-cm visual analogue scale by asking "Compared to the baseline status (before treatment), what is the percentage of improvement for your primary laryngeal symptom?" (0 cm, no improvement or worse; 10 cm, 100% improvement) at weeks 4, 8, and 12 during the treatment.[3] The secondary outcome was the change in total reflux symptom index (RSI) score measured from baseline to every week during the treatment period. The RSI is a nine-item self-administered disease-specific questionnaire that measures symptom severity.[19] The Chinese RSI was translated and back-translated with linguistic and cultural adaptation, and has been validated with good test–retest reliability (intraclass correlation coefficient = 0.79), good internal consistency (Cronbach alpha = 0.73), and good responsiveness (effect size = 1.06) in a sample of Taiwanese patients with suspected LPR.[20]

Statistical Analysis

The subjects were stratified based on the presence/absence of CTRS for baseline characteristics. Pearson chi-square tests were used for dichotomous variables, whereas *t* tests were used for continuous variables. Differences between the proportions of responders in the positive and negative cpH groups were analyzed based on the presence or absence of CTRS. Multivariate logistic regression adjusted for age, gender, body mass index, and the presence of reflux esophagitis was used to assess differences in the numbers of responders between the positive and negative cpH groups at 4, 8, and 12 weeks. Mixed models for repeated measures were used to compare weekly changes in RSI scores between the positive and negative cpH groups. A P value of <.05 was considered significant. The power of this study was calculated using Fleiss Statistical Methods for Rates and Proportions (http://www.sph.emory.edu/~cdckms/sample%20size%202%20grps%20cohort.htm).

RESULTS

Flow of Participants

A total of 262 subjects were assessed for eligibility. One hundred seven subjects participated, and 94 completed the trial (Supplementary Fig. 1). Thirteen patients were excluded from the study due to loss of follow-up (two cases), withdrawal of consent (eight cases), and protocol violation (three cases). There were no differences in the baseline characteristics between nonparticipants and participants. Median adherence in those who completed the study assessed by pill counts was 95% (interquartile range, 91%–100%).

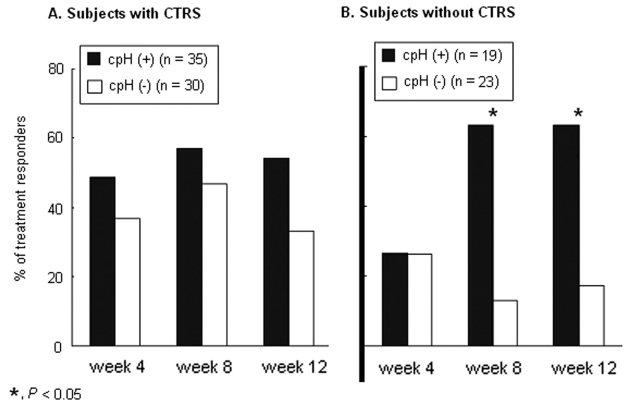

Fig. 1. Comparisons between the composite pH $(cpH)^+$ and cpH^- groups for the percentage of esomeprazole treatment responders, that is, ≥50% reduction in primary laryngeal symptoms of (A) subjects with concomitant typical reflux syndrome (CTRS) and (B) subjects without CTRS.

Baseline Characteristics

The mean age of participants was 50 years (standard deviation = 12.8), and 54% were men (Table I). Among subjects with CTRS, those who were cpH positive were older (53 years vs. 46 years, $P < .05$), had a higher body mass index (25 kg/m^2 vs. 23 kg/m^2, $P < .05$), and had a greater prevalence of reflux esophagitis (36% vs. 10%, $P < .05$) than those who were cpH negative. There were no differences in these characteristics between positive and negative pH groups among subjects without CTRS.

Primary and Secondary Outcomes

Among the participants without CTRS, more responders were found in the positive cpH group than in the negative cpH group after 8 and 12 weeks (63% [12/19] vs. 13% [3/23], $P = .001$; 63% [12/19] vs. 17% [4/23], $P = .004$). However, no difference was found after 4 weeks of treatment (Fig. 1B). There were also no differences between groups in those with CTRS (Fig. 1A). After adjustment, the participants who were cpH positive were 10.3-fold (95% confidence interval [CI], 1.7–61.5; $P = .01$) and 7.9-fold (95% CI, 1.4–44.8; $p = .02$) more likely to respond to esomeprazole after 8 and 12 weeks, respectively, than those who were cpH negative among participants without CTRS (Table II). However, no differences were found between groups in those with CTRS. Weekly measures of changes in RSI scores from baseline also consistently showed that the participants who were cpH positive improved more than those who were cpH negative, particularly in those without CTRS (Fig. 2).

TABLE I.
Baseline Characteristics of the Study Subjects With and Without Concomitant Typical Reflux Syndrome.

	Subjects With CTRS,* n = 65		Subjects Without CTRS, n = 42	
Characteristics	cpH$^+$,† n = 35	cpH$^-$, n = 30	cpH$^+$,† n = 19	cpH$^-$, n = 23
Demographics				
Age, yr	52.8 ± 15.6‡	45.7 ± 9.4	49.1 ± 10.2	51.3 ± 12.9
Male gender	22 (62.9)	13 (43.3)	13 (68.4)	10 (43.5)
Body mass index, kg/m^2	24.9 ± 3.9§	22.5 ± 3.3	23.9 ± 3.2	23.4 ± 4.1
Major complaint of laryngeal symptoms				
Globus sensation	8 (22.9)	8 (26.7)	4 (21.1)	10 (43.5)
Sore throat	6 (17.1)	5 (16.7)	3 (15.8)	4 (17.4)
Hoarseness	10 (28.6)	7 (23.3)	9 (47.4)	7 (30.4)
Cough	9 (25.7)	5 (16.7)	2 (10.5)	1 (4.4)
Throat clearing	2 (5.7)	5 (16.7)	1 (5.3)	1 (4.4)
24-hour pH test				
Excessive distal esophageal acid reflux	29 (82.9)	0 (0.0)	16 (84.2)	0 (0.0)
Excessive pharyngeal acid reflux	15 (42.9)	0 (0.0)	4 (21.1)	0 (0.0)
Endoscopic findings				
Reflux esophagitis	13 (37.1)§	2 (6.7)	5 (27.8)	3 (13.0)
Hiatus hernia	8 (22.9)	3 (10.0)	1 (5.6)	1 (4.4)
Peptic ulcer	6 (17.1)	3 (10.0)	1 (5.6)	4 (17.4)
Helicobacter pylori	8 (29.6)	5 (23.8)	3 (20.0)	2 (14.3)
Laryngeal symptoms and signs at baseline				
Reflux finding score‖	6.7 ± 2.9	5.2 ± 3.1	6.2 ± 2.5	6.1 ± 2.5
RSI score ¶	20.0 ± 8.5	19.3 ± 6.0	15.4 ± 7.4	12.8 ± 6.2

Continuous variables are expressed as mean ± standard deviation. Percentage of subjects is shown in parentheses.
*CTRS is defined as regurgitation or heartburn at least twice a week with mild symptom, or once a week with moderate/severe symptom.
†cpH$^+$ is defined as the presence of 1) excessive pharyngeal acid reflux, that is, ≥2 episodes of pharyngeal acid reflux; and/or 2) excessive distal esophageal acid reflux, that is, ≥4.6% of acid exposure time with pH <4 at 5 cm above the upper margin of the lower esophageal sphincter.
‡$P < .05$, comparison between cpH$^+$ and cpH$^-$.
§$P < .01$, comparison between cpH$^+$ and cpH$^-$.
‖Reflux-finding score ranges from 0 to 26, with higher scores indicating more severe signs.
¶RSI score ranges from 0 to 45, with higher scores indicating more severe symptoms.
cpH = composite pH; CTRS = concomitant typical reflux syndrome; RSI = reflux symptom index.

Power

We assumed response rates of 60% and 20% in the positive and negative cpH groups, respectively.[21] Accordingly, a sample size of 35 in the positive cpH group and 30 in the negative cpH group among participants with CTRS provided a power of 0.92, and a sample size of 19 in the positive cpH group and 23 in the negative cpH group among those without CTRS provided a power of 0.77 at $\alpha = .05$ (two-sided).

Adverse Events

Esomeprazole was generally well tolerated. There was no serious adverse event requiring emergency care or hospitalization. The most commonly reported adverse events included abdominal fullness, constipation, diarrhea, headache, and dyspepsia.

DISCUSSION

The most striking observation in this study was that the baseline cpH parameter, which incorporated excessive distal esophageal acid exposure and excessive pharyngeal acid reflux, was predictive of PPI therapy response in participants with suspected LPR and without CTRS, but not in those with the syndrome.

The ability of a novel pH test parameter to predict suspected LPR without CTRS, as demonstrated by our findings, may be of clinical value, particularly as treatment approaches tend to vary depending on whether the specialty of the treating physician is laryngology or gastroenterology.[2,22] Most placebo-controlled trials that adopted either esophageal or pharyngeal pH parameters as predictors of PPI treatment response did not find any predictive value.[3] Moreover, these studies had a small sample size (21–39 participants). A larger open-label trial of 82 subjects conducted by Park el al.[23] found that both distal and proximal esophageal acid refluxes in both upright and supine positions at the baseline were marginally and statistically nonsignificantly higher among PPI treatment responders than those among nonresponders. Oelschlager et al.[24] conducted an open-label trial with a combination of laryngoscopy and pharyngeal pH probe in 76 subjects with suspected LPR. They reported that 88% of the subjects with an abnormal reflux-finding score and an abnormal pharyngeal pH improved with antireflux therapy compared with only 44% of the subjects with a normal reflux-finding score

TABLE II.
Comparison of Primary Outcomes Between Subjects With and Without Abnormal Composite pH, Stratified by the Presence or Absence of Concomitant Typical Reflux Syndrome.

	Subjects With CTRS, n = 58				Subjects Without CTRS, n = 36			
Composite pH	No.	Responders, No. (%)	Adjusted OR [95% CI]	*P*	No.	Responders, No. (%)	Adjusted OR [95% CI]	*P*
Week 4								
cpH^+	31	16 (51.6)	1.8 [0.5–6.2]	.33	18	5 (27.8)	0.1 [0.005–1.7]	.11
cpH^-	27	9 (33.3)			18	5 (27.8)		
Week 8								
cpH^+	31	19 (61.3)	2.8 [0.8–10.1]	.11	18	12 (66.7)	10.3 [1.7–61.5]	.01
cpH^-	27	13 (48.2)			18	3 (16.7)		
Week 12								
cpH^+	31	19 (61.3)	3.1 [0.9–10.7]	.07	18	12 (66.7)	7.9 [1.4–44.8]	.02
cpH^-	27	10 (37.0)			18	4 (22.2)		

ORs were adjusted for age, gender, body mass index, and the presence of reflux esophagitis.
CI = confidence interval; cpH = composite pH; CTRS = concomitant typical reflux syndrome; OR = odds ratio.

and pH probe. Taken together, these findings suggest that either esophageal or pharyngeal pH alone is not sufficient for a diagnosis. In this study, we used a cpH parameter, incorporating both esophageal and pharyngeal pH, and found that the odds ratio (3.8; 95% CI, 1.6–9.0) for the cpH parameter was larger than that for the esophageal (2.8; 95% CI, 1.2–6.5) or pharyngeal (2.0; 95% CI, 0.7–6.2) pH parameter in the prediction of PPI treatment response (Supplementary Table I), reflecting a direct involvement of pharyngeal injury and an indirect involvement of esophageal stimulation with vagal reflex. This concept was further supported by a recent study using a pH impedance test to predict PPI treatment responders in 92 subjects, showing that both increased distal esophageal acid exposure and increased pharyngeal bolus exposure time, including nonacidic refluxate, may predict PPI treatment response.[25]

Although it is reasonable to speculate that the presence of CTRS suggests the cause of chronic laryngitis, there are few data regarding whether CTRS can predict PPI treatment response.[23,26] Furthermore, it is also possible that CTRS is a bystander of chronic laryngitis in a subset of patients, because both are common diseases. As such, abnormal pH results may simply reflect CTRS, and thus, the diagnostic accuracy of a pH test may be compromised by the presence of CTRS. This may explain our finding that pH results among participants without CTRS had a superior predictive value compared with those obtained from patients with CTRS. However, the usefulness of the pH tests has rarely been evaluated in patients with suspected LPR and without CTRS, except in the aforementioned study by Vaezi el al.[7] Two analogous controlled trials were performed in patients with uncontrolled asthma and unexplained cough, respectively. Mastronarde et al. evaluated the therapeutic efficacy of esomeprazole among 412 subjects with inadequately controlled asthma and without CTRS.[27] They found that 40% of subjects who underwent 24-hour esophageal pH test had abnormal distal esophageal acid exposure but it did not predict treatment response. One may argue that a high prevalence of abnormal acid reflux in asthmatics without CTRS may in part be explained by an effect rather than a cause of asthma, that is, hyperinflation of lungs may increase the pressure gradient between the abdomen and thorax, resulting in impaired barrier function.[28] Recently, Shaheen et al.[29] found no therapeutic benefit of PPI over a placebo in 40 patients with unexplained cough and without CTRS. However, in their subgroup analyses, the cough-specific quality of life score, the primary outcome, was significantly improved in the subgroup with excessive distal esophageal acid exposure, but not in the subgroup with normal distal esophageal acid or in the placebo treatment groups, suggesting a possible predictive role of pH in patients without CTRS.

We also analyzed the findings of laryngoscopy, upper gastrointestinal endoscopy, and CTRS and found that none of them predicted a treatment response (Supplementary Table I). Limited data are available for CTRS and reflux esophagitis in the prediction of

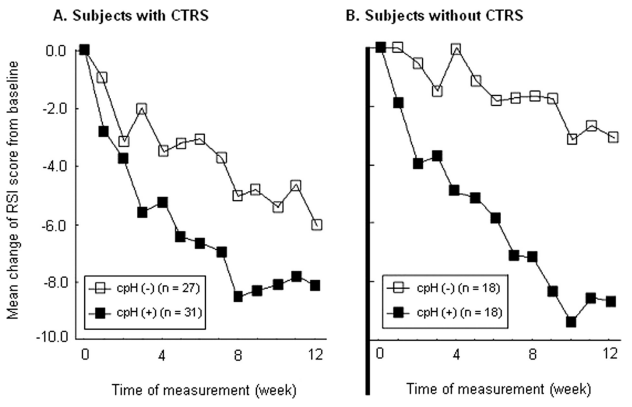

Fig. 2. Comparisons between composite pH $(cpH)^+$ and cpH^- groups for mean change in reflux symptom index (RSI) score from baseline in subjects with suspected laryngopharyngeal reflux. (A) subjects with concomitant typical reflux syndrome (CTRS; $P = .03$ for mixed model); (B) subjects without CTRS ($P = .006$ for mixed model).

treatment response.[30] However, the lack of association between the treatment response and baseline reflux finding score, and between change of reflux finding score and RSI score (data not shown) in this study are consistent with the results of most controlled trials,[3] probably due to the nonspecificity of laryngeal signs for the diagnosis,[31] or insufficient time for detecting improvements of laryngoscopic findings.[13]

The present study had several strengths. First, to minimize the possibility of overdiagnosis, we excluded subjects with common etiologies of chronic laryngeal symptoms other than reflux such as chronic rhinosinusitis or allergies,[32] and those with psychiatric problems.[9] Second, based on these strict exclusion criteria, we selected 107 participants out of 262 potential candidates, which is a relatively large sample size compared with similar studies. Third, the definition of a responder as the clinical relevant outcome in combination with the disease-specific validated questionnaire (RSI) with repeated measures used in this study may support the validity and the reliability of patient-reported outcomes.

Our study also had several limitations. This was not a randomized placebo-controlled trial; thus, a biased outcome should be considered. However, the weakness should have been minimized by the blindness of both patients and investigators to the results of pH test and upper gastrointestinal endoscopy throughout the study period. In addition, the consistent improvements of primary laryngeal symptoms, along with the similar results of longitudinal RSI measurements, suggest that our findings are not biased. Furthermore, our study results may provide a rationale for recruiting prespecified subjects in future placebo-controlled trials. Second, a lack of uniform or accepted universal criteria of abnormal pharyngeal pH may limit the widespread clinical use of the cpH parameter.[33] However, using the strict criterion developed by Williams et al.[17] to define the pharyngeal acid reflux event described, we have recently found a percentage agreement of 98% (Cohen kappa = 0.96) between two experienced raters, indicating a good reliability of this parameter.[14] In addition, we used the criterion of $\geq$2 events of pharyngeal acid reflux to define abnormality based on a set of published normal data acquired using the same pH technique.[18] Further studies are needed to confirm our findings. Third, these results were obtained from a selected referral population and may not be generalized to patients with LPR in a primary care setting.

CONCLUSION

We found that a cpH parameter, which incorporated excessive pharyngeal acid and excessive distal esophageal acid, predicted response to PPI therapy among patients with laryngeal symptoms but without CTRS. We therefore recommend evaluation of the pH parameter prior to initiation of PPI treatment in patients with suspected LPR and without CTRS. Future randomized placebo-controlled trials adopting this parameter as an inclusion criterion are warranted.

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